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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,958	02/03/2004	Robert Charles Downs	36-001911US	3828
29490	7590	09/07/2007		
GENOMICS INSTITUTE OF THE NOVARTIS RESEARCH FOUNDATION 10675 JOHN JAY HOPKINS DRIVE, SUITE E225 SAN DIEGO, CA 92121-1127			EXAMINER BOWERS, NATHAN ANDREW	
			ART UNIT 1744	PAPER NUMBER
			NOTIFICATION DATE 09/07/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPLegal@gnf.org
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Office Action Summary	Application No. 10/771,958	Applicant(s) DOWNS ET AL.	
	Examiner Nathan A. Bowers	Art Unit 1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-85 is/are pending in the application.
- 4a) Of the above claim(s) 1-41 and 80-85 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 42-79 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>043004, 020304</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claims 42-79 in the reply filed on 06 July 2007 is acknowledged.

Claims 1-41 and 80-85 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07 July 2007.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 1) Claims 42, 48-51, 59-61 and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Hitzman (US 4519984).

With respect to claims 42 and 59-61, Hitzman discloses a method of fermenting a plurality of samples by providing a plurality of sample vessels (Figure 2:52) in a container frame (Figure 2:54). Fermenting is accomplished in part by simultaneously delivering gas to each of the sample vessels using a plurality of cannulas (Figure 1:18) associated with the sample vessels. Each of the cannulas is associated with a fermenter head (Figure 2:60) that comprises a manifold through which air is dispersed

from a common source to the individual cannulas that are in communication with a specific vessel. This is described in column 2, line 51 to column 3, line 60.

With respect to claims 48 and 62, Hitzman discloses the method in claims 42-59 wherein air or an oxygen containing gas is added to each of the vessels. Hitzman discloses that aerobic fermentation procedures are well known in the art.

With respect to claims 49 and 50, Hitzman discloses the method in claim 42 wherein gas comprising air and oxygen is added to the samples over time. Since the microorganisms consume oxygen during aerobic fermentation, the ratio of air to oxygen will inherently increase unless heavy sparging is continued. Aerobic fermentation processes that involve a decrease in oxygen concentration levels at various rates as a result of cellular metabolism are well known in the art.

With respect to claim 51, Hitzman discloses the method in claim 42 wherein the sample vessels are arranged in a linear array. This is apparent from Figure 2.

With respect to claim 79, Hitzman discloses the method in claim 79 wherein the sample vessels in the container frame are positioned in a water bath designed to control the temperature of the vessels. This is disclosed in column 3, lines 44-47.

2) Claims 42, 44-51, 53-56, 59-61 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Arad (US 5534417).

With respect to claims 42 and 59-61, Arad discloses a method of fermenting a plurality of samples wherein a plurality of sample vessels (Figure 1:5 and Figure 1:6) are arranged in a container frame comprising vertical posts (Figure 1:2), a base (Figure

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1:3) and horizontal upper element (Figure 1:4). Column 4, lines 50-55 and column 5, lines 11-31 state that a gas is moved through a manifold located inside the horizontal upper element in such a way that the gas is simultaneously delivered to each of the vessels using a plurality of cannulas (Figure 1:7).

With respect to claims 44-47, Arad discloses the method in claim 42 wherein the samples undergo processing following the completion of fermentation. Column 7, lines 32-46 state that half of the cell solution is withdrawn from the vessels through a fluid outlet (Figure 1:9) and delivered to a conical tank. The cells are allowed to settle and precipitate at the bottom of the tank. The upper fraction from the tank is then returned to the cell solution remaining in the vessels using a recycling technique that involves aspiration (suction).

With respect to claims 48 and 62, Arad discloses the method in claims 42 and 59 wherein air (and therefore oxygen) is added to the samples. This is disclosed in column 5, lines 11-18.

With respect to claims 49 and 50, Arad discloses the method in claim 42 wherein gas comprising air and oxygen is added to the samples over time. Since the algae produce oxygen during their growth, the ratio of air to oxygen will inherently decrease unless heavy sparging of air and carbon dioxide is continued. Plant cell culturing processes that involve an increase in oxygen concentration levels at various rates as a result of cellular metabolism are well known in the art.

With respect to claim 51, Arad discloses the method in claim 42 wherein the sample vessels are arranged in either a linear array or a rectangular array. Arad suggests the use of a 4 X 30 array of cells in column 7, lines 13-21.

With respect to claims 53-56, Arad discloses the method in claim 42 wherein the concentration of cells, the concentration of cellular products, and temperature are all monitored throughout the entire culturing process. This is disclosed in column 7, lines 25-46 and column 8, lines 38-42. Accordingly, sensors must inherently have been coupled to the sample vessels. The use of environmental control systems during fermentation is considered to be notoriously well known in the art. The detection and estimation of cell concentration in a culture medium is typically accomplished by measuring the optical density of the medium.

With respect to claim 63, Arad discloses the method in claim 59 wherein anaerobic fermentation is accomplished by delivering an inert gas to maintain anaerobic fermentation conditions in the sample vessels. Specifically, Arad teaches that his method is generally used to culture algae cells that do not require oxygen to undertake photosynthesis. Nitrogen gas in the air added to the vessels is an inert gas that maintains anaerobic conditions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3) Claims 43, 64-67, 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Hitzman (US 4519984) or Arad (US 5534417) each as applied to claims 42 and 59.

With respect to claims 43 and 64-67, Hitzman and Arad disclose the methods set forth in claims 42 and 59 as set forth in the 35 U.S.C. 103 rejections above. In column 4, lines 44-46, Hitzman discloses the use of cylindrical fermentation vessels having

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volumes as low as 116 ml (0.5 inches in diameter and 3 feet in length). In column 3, line 65 to column 4, line 5, Arad discloses the use of cylindrical fermentation vessels having volumes as low as 200 ml (5 cm in circumference and 10 cm in length).

Although Hitzman and Arad do not disclose the use of vessels that have capacities lower than 100 ml, it would have been obvious to construct them in this way if it was determined that a collection of smaller bioreactors would have been more efficient in the production cells and cell products. The selection of a bioreactor volume is a result effective variable that is optimized through routine experimentation. See MPEP 2144.05.

With respect to claims 77 and 78, Hitzman and Arad disclose the methods set forth in claim 59 as set forth in the 35 U.S.C. 103 rejections above. Hitzman teaches in column 5, lines 3-6 that bioreactors are provided as an array of 50 units. In column 7, lines 13-21, Arad offers an example in which the bioreactors are arranged in a 4 X 30 array. Although Hitzman and Arad do not expressly disclose the use of an 8 by 12 array or an array that comprises 96, 384 or 1536 vessels, it would have been obvious to rearrange the systems of Hitzman and Arad in this way if it was determined that 96, 384 or 1536 were needed for a specific operation. Clearly, Hitzman and Arad both disclose that their systems are capable of accommodating a large number of bioreactor units. It would require only minor alterations in the methods of Hitzman and Arad in order to incorporate 96, 384 or 1536 vessels.

4) Claims 52, 57, 58 and 68-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hitzman (US 4519984) as applied to claims 42 and 59, and further in view of Powell (US 6066497).

With respect to claims 52 and 68-76, Hitzman discloses the method set forth in claims 42 and 59 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly state that the reaction vessels are moved to a processing station that includes a centrifuge and an aspirator head.

Powell discloses a processing station for a plurality of bioreactor vessels (Figure 1:6). The processing station rotates the vessels according to a centrifugal motion about a horizontal axis (Figure 2:4). The vessels are equipped with a distribution assembly capable of sucking fluid from each of the vessels or delivering fluid to the vessels using a plurality of tubes (Figure 1:9). This is disclosed in column 1, lines 39-60 and in column 3, line 64 to column 4, line 67.

Hitzman and Powell are analogous art because they are from the same field of endeavor regarding cell culture apparatuses.

At the time of the invention, it would have been obvious to further process the bioreactor vessels disclosed by Hitzman using the system disclosed by Powell. Powell teaches in column 1, lines 9-35 that subjecting a bioreactor vessel to continuous rotation is beneficial because the rotation serves to facilitate mixing while ensuring that cells remain bathed in the culture medium. The addition and aspiration of liquids to and from a culture vessel during fermentation and during post processing stages is considered to be well known in the art.

With respect to claims 57 and 58, Hitzman discloses the method set forth in claim 42 as set forth in the 35 U.S.C. 102 rejection above. Hitzman, however, does not expressly indicate that the vessels are autoclaved.

Powell discloses the method as previously described above. In addition, Powell teaches in column 7, lines 20-27 that the bioreactor vessels are heat sterilized.

At the time of the invention, it would have been obvious to autoclave the plurality of sample vessels disclosed by Hitzman. Powell indicates that it is important to sterilize bioreactor components prior to fermentation in order to remove any biological contaminants from the system. Autoclaves are considered to be well known in the art as effective means to accomplish heat sterilization.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Shaaltiel (US 20020110915) reference discloses the state of the art regarding the use of a plurality of cannulas to simultaneously deliver a gas to a plurality of sample vessels. See Figure 6a and Figure 6b.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone


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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



NAB



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